

California M E D I C I N E

OFFICIAL JOURNAL OF THE CALIFORNIA MEDICAL ASSOCIATION

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VOL. 69

OCTOBER, 1948

No. 4

BAL (2,3-Dimercaptopropanol) in the Treatment of Massive Overdosage with Mapharsen

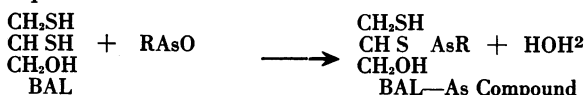
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BRITISH anti-lewisite, familiarly known as BAL, was developed during the last war as an antidote for the arsenical blister gases. Although distributed to troops principally in the form of ointment to be applied in case of conjunctival or cutaneous exposure, BAL has now been shown valuable in the treatment of systemic poisoning with arsenic, gold, mercury, cadmium, and lead. Most of these applications were suggested by the extensive studies carried on in Britain and in this country. Some of the information gained in these investigations has been released in the form of large symposia, the component parts of which concern the biochemistry,³ toxicology, pharmacology and experimental therapeutics,¹⁸ and clinical uses¹⁷ of BAL.*

MODE OF ACTION OF BAL

Peters, Stocken, and Thompson²¹ advanced the fundamental concept that agents which combine with and inactivate the sulfhydryl groups of the activating proteins of enzyme systems, will interfere with the activity of those systems. Thus the pyruvate oxidase system²⁵ was found to depend upon the SH groups for its activity, and trivalent arsenicals were found to attack particularly those enzymes responsible for carbohydrate and fat metabolism.²⁶ At first, thiamine¹³ and para-aminobenzoic acid²⁴ were used in an attempt to stimulate the disabled cellular economy. More promising was the finding²⁵ that arsenic and other heavy metals could be "detoxified" by giving compounds (particularly those with sulfhydryl

groups), whose thiol groups exerted a greater affinity for arsenic than that possessed by the attacked tissue thiols. Dithiol compounds particularly were able to form a relatively stable, non-toxic, ring form thioarsenate which appeared promptly in the urine.^{3a} A simple aliphatic dithiol, 2, 3-dimercaptopropanol (BAL), some of the BAL glucosides, and certain of the monothiols were the most useful of some 44 mercaptans tested in this regard.¹² The reaction is thought to be abetted by the similar spacial relationships of the SH radicals in the antidote and in the tissue proteins from which the heavy metal is displaced.²⁶ The reaction of arsenic with BAL may be represented as:



It seems very probable that other heavy metals besides arsenic combine with tissue proteins to interfere with tissue respiration,¹⁴ and also that they may be attracted from the tissue proteins by BAL with which they form excretable compounds. In this group may be included antimony, bismuth (although urinary excretion does not rise); chromium, mercury, nickel,^{18g} cadmium,^{18f} vanadium, lead, stibium, and zinc.²⁹

CHARACTERISTICS AND TOXICITY OF BAL:

2, 3-dimercaptopropanol is a colorless liquid with the typical skunk-like odor of the mercaptans. It is soluble in oil with the aid of a solubilizing agent such as 20 per cent benzyl benzoate, but it may also be prepared in an ointment base for percutaneous administration. On the skin BAL is painful, may form wheals,^{17e} and cutaneous sensitization has occurred.²⁶

From the Medical Service, Letterman General Hospital. The opinions expressed in this paper are those of the authors, and do not necessarily reflect the official opinion of the Medical Department of the United States Army.

*BAL in a 10 per cent solution in 20 per cent peanut oil is available commercially.

California M E D I C I N E

OWNED AND PUBLISHED BY THE CALIFORNIA MEDICAL ASSOCIATION
450 SUTTER, SAN FRANCISCO 8 PHONE DOUGLAS 2-0062

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EDITORIAL

November 2, 1948

Californians will have a chance, along with the rest of the nation, to cast their ballots on November 2 on the pros and cons of candidates and issues. The ballot in this state will be a long one, due to the presence of 19 propositions which have been placed before the electorate under the initiative and referendum laws of the state.

Heading the list on the ballot will be the candidates for President of the United States, with Harry S. Truman and Thomas E. Dewey vying for top honors. (Henry Wallace, the Communist candidate, the Dixiecrat candidate and others need no further consideration here.) Mr. Truman has consistently echoed the late FDR's sentiments concerning a system of state medicine; Mr. Dewey has been positive and strong in his assertions that a system of private medical practice is better and more beneficial to the people than a government-controlled system. Doctors may make their own choice between the two.

Next come the candidates for Congress and the State Legislature and in some districts there will be hot contests. The California Medical Association makes it a policy not to sponsor individual candidates but there is no avoiding the preference which physicians are likely to show for one or another contestant because of his views on the private enterprise system or a firmly-controlled system of governmental paternalism and professional slavery. The doctors in each district are aware of the proclivities of their own candidates and will vote accordingly.

State propositions will follow the list of candidates for office. There will be 19 of these and there would have been 20 if the State Supreme Court had not voted unanimously last month to throw out the so-called "Omnibus" or "Bill of Rights" initiative. This

bill would have amended 15 of the 25 articles of the State Constitution, a fact which the Supreme Court held to be a virtual revision of the Constitution. Such revision is permitted only by a Constitutional Convention. The bill would, among other things, have placed the licensing and control of all the healing arts professions under a board of five "naturopathic physicians," a quaint term for a chiropractor who wishes to gain a new title and new authority by passing a law. The potential spectacle of a board of five chiropractors passing on the professional qualifications of doctors of medicine was not overlooked by the Supreme Court. The justices, by unanimous vote, decided that this issue was not to go before the voters; in so doing they eliminated what promised to be a tough fight for the physicians and for all other business and professional interests in the state, a fight for right and justice against the emotionalism engendered in special interest groups of old-age pensioners, partly-trained professional men, professional sob-sisters and others whose legislative programs have failed of accomplishment before the tribunal of the State Legislature.

Of the remaining ballot propositions, Number 4 and Number 13 appear to be of greatest interest to physicians. Number 4 is the so-called "McLain Bill" to increase pensions to the aged, to control the payments of assistance to the blind and to provide a different system of hospitalization for recipients of state aid. The bill would alter the present system of medical care in county hospitals, would permit various practitioners to serve on county hospital staffs and would permit the acceptance of many cases by county hospitals regardless of the ability of the patient to pay for his own care. The California Medical Asso-

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NOTICES AND REPORTS

New California Medical Association Constitution and By-Laws

The following is a tentative draft of a proposed revision of the Constitution and By-Laws of the California Medical Association. Work on the revision was undertaken first by a committee of 16 authorized by the 1947 House of Delegates to review the existing document. That committee's draft was referred to a committee of five by the 1948 House of Delegates for further study.

Comments and suggestions by C.M.A. members, which are solicited by the committee, should be addressed: Committee on Constitution and By-Laws, Sam J. McClendon, M.D., chairman, California Medical Association, 450 Sutter Street, San Francisco 8.

CONSTITUTION

ARTICLE I.—NAME, PURPOSES AND ORGANIZATION

Section 1.—Name

The name of this organization is California Medical Association (hereinafter referred to as the Association).

Section 2.—Purposes

The purposes of this Association are to promote the science and art of medicine, the protection of public health, and the betterment of the medical profession; to promote similar interests of its component societies; and to unite with similar organizations in other states and territories of the United States to form the American Medical Association.

Section 3.—Organization

This Association has two divisions: One, the Association as an organization; and Two, the Scientific Assembly. The Association as an organization includes component societies and their active members, the House of Delegates, Council, Commissions

and Standing Committees. The Scientific Assembly includes all members of the Association and the scientific sections.

Section 4.—Definition of Component Societies

Component societies include all county medical societies (which may cover one or more counties) heretofore or hereafter chartered by this Association.

Section 5.—Component Society Charters

Charters to component societies may be granted and revoked as hereinafter prescribed, subject to the limitation that only one charter may be outstanding at any one time in any county.

ARTICLE II.—MEMBERSHIP

Section 1.—Classes of Members

The members of this Association shall consist of Active, Associate, Honorary, Retired, Life and Affiliate members.

Section 2.—Membership Qualifications, Rights, Privileges, Duties and Method of Election

The qualifications, rights, privileges, duties, obligations and methods of election of the several classes of membership are as stated in the By-Laws.

County Society Secretaries' Conference

A conference of secretaries of the component medical societies of the California Medical Association, the first since the entrance of the United States into the war, will be held February 4 and 5, 1949, in San Francisco. Formerly such conferences were held annually. Date for the 1949 conference was set by the Executive Committee of C.M.A. at a meeting in August.